CAVERDOCK: A NEW TOOL FOR ANALYSIS OF LIGAND BINDING AND UNBINDING BASED ON MOLECULAR DOCKING

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Understanding the protein-ligand interactions is crucial for engineering improved catalysts. The interaction of a protein and a ligand molecule often takes place in enzymes active site. Such functional sites may be buried inside the protein core, and therefore a transport of a ligand from outside environment to the protein inside needs to be understood. Here we present the CaverDock [1], implementing a novel method for analysis of these important transport processes. Our method is based on a modified molecular docking algorithm. It iteratively places the ligand along the tunnel in such a way that the ligand movement is contiguous and its energy is minimized. The output of the calculation is ligand trajectory and energy profile of transport process. CaverDock uses a modified version of the program AutoDock Vina [2] for molecular docking and implements a parallel heuristic algorithm to search the space of possible trajectories. Our method lies in between of geometrical approaches and molecular dynamics simulations. Contrary to geometrical methods, it provides an evaluation of chemical forces. However, it is not as computationally demanding as the methods based on molecular dynamics. The typical input of CaverDock requires setup for molecular docking and tunnel geometry obtained from Caver [3]. Typical computational time is in dozens of minutes at a single node, allowing virtual screening of a large pool of molecules. We demonstrate CaverDock usability by comparison of a ligand trajectory in different tunnels of wild type and engineered proteins; and computation of energetic profiles for a large set of substrates and inhibitors. CaverDock is available from the web site http://www.caver.cz.

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